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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/058,069	01/29/2002	Gary R. Braslawsky	0280727 2001-30-0080CP1	2502

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EXAMINER	
BLANCHARD, DAVID J	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 11/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/058,069	BRASLAWSKY ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20,29,38-40,62,63,75-80 and 84-101* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20,29,38-40,62,63,75-80 and 84-101* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/6/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 05 September 2006 has been entered.

2. Claims 1-19, 21-28, 30-37, 41-61, 64-74 and 81-83 are cancelled.

Claims 20, 29, 38-40, 62, 75-80, 85-92, 95-96 and 99-100 have been amended.

Claim 101 has been added.

3. Claims 20, 29, 38-40, 62-63, 75-80 and 84-101 are pending and under examination.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on 06 April 2006 has been fully considered by then examiner. A signed copy of the IDS is included with this Office Action.

Rejections Withdrawn

6. The rejection of claims 55, 68 and 81 under 35 U.S.C. 103(a) as being unpatentable over Gillies et al (Human Antibodies and Hybridomas, 1(1):47-54, 1990, cited previously) as evidenced by the specification in view of Kashmiri et al (WO 00/26394, 5/11/00) and Anderson et al (U.S. Patent 6,348,581 B1, priority at least to 2/18/1998, cited previously) and Thorpe et al (U.S. Patent 6,342,219 B1, 4/28/1999, cited previously) is withdrawn in view of the cancellation of the claims.

Response to Arguments

7. The rejection of claims 20, 29, 38-40, 62-63, 75-80 and 84-101 under 35 U.S.C. 103(a) as being unpatentable over Gillies et al (Human Antibodies and Hybridomas, 1(1):47-54, 1990, cited previously) as evidenced by the specification in view of Kashmiri et al (WO 00/26394, 5/11/00) and Anderson et al (U.S. Patent 6,348,581 B1, priority at least to 2/18/1998, cited previously) and Thorpe et al (U.S. Patent 6,342,219 B1, 4/28/1999, cited previously) is maintained.

The response filed 9/5/2006 summarizes the examiners arguments in the Final office Action mailed 3/3/2006 and the Advisory Action mailed 7/19/2006. Applicants arguments are summarized as follows: Gillies either alone or in combination with the secondary references provides no suggestion or motivation to produce the purified dimeric, tetravalent (H_4L_4), CH2 domain-deleted antibodies of the claimed invention. According to applicant, at the time the invention was made, one of ordinary skill in the art did not know that dimeric CH2 domain-deleted antibodies of the claimed invention even existed and there was no reasonable expectation that standard antibody

purification methods would successfully purify dimeric, tetravalent (H_4L_4), CH2 domain-deleted antibodies of the claimed invention. Applicants' arguments have been fully considered but are not found persuasive. The examiner is not arguing that the references teach the production of purified dimeric, tetravalent (H_4L_4), CH2 domain-deleted antibodies of the claimed invention, the examiner is arguing that for the reasons set forth below (and different from applicants reasons), it would have been *prima facie* obvious to one of ordinary skill in the art to produce a CH2 domain-deleted antibody identical to the presently claimed CH2 domain-deleted antibody, and purify the antibody. For example, Kashmiri et al teach purification of the CC49 antibodies "according to standard procedures in the art" to at least about 90-95% homogeneity or more preferably 98-99% or more homogeneity (pg. 17, lines 20-24) and Thorpe et al teach antibody pruification using the techniques disclosed in the present application, i.e., protein G and HPLC columns (e.g., Thorpe at col. 61, lines 10-19). Thus, the desireability of purifying the humanized CC49 CH2 domain-deleted antibodies as taught by Gillies et al and Kashmiri et al and Anderson et al and Thorpe et al, is made explicit in the references, particularly for therapeutic purposes in cancer patients.

The examiners second point is that products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, absent objective evidence to the contrary, the purified CH2 domain-deleted antibodies of the prior art would

"spontaneously assemble or associate into stable dimeric constructs or tetravalent antibodies." (i.e., dimeric, tetravalent (H_4L_4), CH2 domain-deleted antibodies) (specification at pg. 24, lines 7-9, and also pg. 7, lines 18-20).

In response to applicant's argument that the prior art does not recognize the dimerization properties of the claimed invention, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). It is reiterated that, one of ordinary skill in the art would have been motivated and had a reasonable expectation of success to modify the CH2 domain deleted mouse antibody (B72.3) of Gillies et al in which the CH3 domain of the human gamma-1 constant region is fused directly to the hinge region with the humanized CC49 VH and VL sequences taught by Kashmiri et al to reduce the immunogenicity of the CH2 domain deleted antibody and enhance the therapeutic index of the CH2 domain deleted antibody as a targeting element for delivering various cytotoxic agents for human cancer therapy as taught by Anderson et al and Thorpe et al. Further, the teachings of Anderson et al and Thorpe et al are evidence that it was known and routine in the art at the time the instant invention was made to conjugate cytotoxic agents to an antibody for targeting and the art of Kashmiri et al teach that the humanized CC49 antibody comprising the heavy chain variable region of SEQ ID NO:7 and the light chain variable region of SEQ ID NO:9 retained specificity for the CC49 antigen. Thus, there was a reasonable expectation of success in making the above modifications. Therefore, the CH2 domain

deleted CC49-specific antibody comprising the heavy and light chain variable regions sequences of SEQ ID Nos:7 and 9, respectively, wherein the CH3 domain of the human gamma-1 constant region is fused directly to the hinge region of the prior art is identical to the claimed CH2 domain deleted CC49-specific antibody and the CH2 domain deleted CC49-specific antibody of the prior art would necessarily non-covalently associate into a tetravalent dimeric CH2 domain deleted CC49-specific antibody, as this is merely an intrinsic property of the CH2 domain deleted CC49-specific antibody of the claimed invention. Applicant is reminded that products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433. See also Titanium Metals Corp. v. Banner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir.

1985). Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art... However, "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). See MPEP 2112.

Applicants' arguments that Gillies performed HPLC size exclusion chromatography on the mixture of antibody produced by their method, yet they did not describe observing the dimeric (H_4L_4, 240 kDa) CH2 domain-deleted anti-TAG-72 antibodies of the claimed invention and thus, provided no motivation to prepare dimeric CH2 domain-deleted anti-TAG-72 antibodies according to their method and then purify from the resulting mixture the dimeric CH2 domain-deleted anti-TAG-72 antibodies of the present invention. This has been fully considered but is not found persuasive. Again, as discussed above the examiner is not arguing that it would have been obvious to one of ordinary skill in the art to produce dimeric CH2 domain-deleted antibodies and then purify the dimeric CH2 domain-deleted antibodies, the examiner is arguing that it would have been obvious to one of ordinary skill in the art to produce and purify the CH2 domain deleted antibody, which would necessarily spontaneously assemble or associate into a stable dimeric tetravalent antibody. Contrary to applicants' arguments, Gillies et al teach that the CH2 domain deleted antibodies were purified by immunoaffinity chromatography on an anti-human k monoclonal antibody-Sepharose

column. Gillies used SDS-PAGE or HPLC to asses the purity of the antibodies not for separation (see pg. 49, top of 1st column).

The examiner acknowledges applicants remarks regarding the unexpected and advantageous increase in antigen binding activity of the claimed dimeric CH2 domain deleted antibody. Applicant is always invited to submit evidence of unexpected results in support of nonobviousness. See MPEP 716. However, given the examiners arguments above, it would be more relevant to submit objective evidence showing that the purified monomeric CH2 domain-deleted antibodies of the prior art would not spontaneously assemble or associate into stable dimeric tetravalent antibodies.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references and the rejections is maintained.

Conclusion

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Braslawsky et al. U.S. Patent 6,897,044

Tankersley D. L. Immunological Reviews, 139:159-172, 1994.

Kleinveld H. A. et al. Scandinavian Journal of Rheumatology Supplement, Suppl. 75 :157-163, 1988.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
David J. Blanchard
571-272-0827